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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,462	09/18/2001	Jeffrey Wilusz	601-1-109N	7730

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EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/17/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/955,462	Applicant(s) WILUSZ ET AL.	
	Examiner David A Lambertson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *14-16 and 22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-13 and 17-21) in Paper No. 13 filed October 7, 2002, is acknowledged.

Claims 14-16 and 22-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Applicant's claim for domestic priority to U.S. provisional application 60/223,682 under 35 U.S.C. 119(e) is not granted. The application is not properly referenced in the declaration.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Specifically, the full residence addresses of each of the inventors have been changed without initialing the changes.

The claim to priority under 35 U.S.C. 119(e) appears to be defective. Specifically, the filing date is listed as September 16, 2000, whereas the actual filing date appears to be September 19, 2000.

Drawings

The drawings have been objected to by the Draftsperson (please see the attached form PTO-948 for details). Applicants are reminded that drawing corrections are no longer held in abeyance. (37 CFR 1.85(a)).

Claim Objections

Claim 3 is objected to because of the following informalities: the claim is grammatically incorrect, stating, "wherein said extract is prepared by dialysis of *a* said extract". Removing the "a" would be remedial. Claim 4 is objected to because it is unclear how the claim further limits the invention, as a mammalian cell lysate must inherently come from a mammalian cell or tissue. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for S100 HeLa cell extracts, does not reasonably provide

enablement for all mammalian cell extracts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of the invention. The invention is a mammalian cytoplasmic extract with the intended use of biochemically measuring the decapping of mRNA species. The invention is novel in that no one had previously been able to detect this activity in mammalian cells.

Scope of the invention. The scope of the invention is very broad, claiming compositions that are comprised of all mammalian cell extracts, for the measurement of mRNA decapping activity. The instant specification is specifically directed towards the use of S100 HeLa cell extracts to measure this activity.

State of the art. The state of the art is very underdeveloped. In fact, the specification states that there "is currently no direct biochemical evidence for decapping in mammalian cells" (see paragraph [0007]). As a result, the skilled artisan cannot turn to the prior art in order to determine what mammalian cell extracts, obtained in what particular manner, can be used to measure the activity of mRNA decapping.

Number of working examples and Guidance provided by applicant. The instant specification only provides guidance and working examples regarding the use of S100 HeLa cell extracts. The specification does not teach what specific cell factors are involved in the reaction, or how to prepare/purify these factors in a method other than the S100 HeLa cell extract. As a result, the skilled artisan can only rely on the specification for guidance concerning the use of S100 HeLa cell extracts, and not any mammalian cell extract prepared in any manner.

Level of skill in the art. The level of skill in the art, concerning the measurement of mRNA decapping in mammalian extracts. is under-developed. No one has previously been able to show this occurs (see paragraph [0007] of the instant specification), therefore, no one else can have an appreciable level of skill with respect to the specific invention.

Unpredictability of the art. The instant specification indicates that the art is highly unpredictable, based on the statement that no one had previously been able to identify mRNA decapping in mammalian cell extracts. Thus, the level of skill in the art is under-developed in terms of measuring mRNA decapping activity in mammalian cell extracts. The instant specification itself only identifies this activity in a specific cellular extract, the S100 HeLa cell extract. Based upon the teachings of the prior art and the instant specification, the skilled artisan would be forced to practice undue trial and error experimentation regarding the measurement of mRNA decapping in mammalian cell extracts other than the S100 HeLa cell extract.

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims read on a composition or kit comprising any mammalian cell cytoplasmic extract, a methylated cap analog and a cap-labeled mRNA substrate, further comprising additional components for detecting mRNA deadenylation and degradation.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe the additional components required for detecting mRNA deadenylation and degradation.

Applicant claims these additional components by function only, without any disclosed or known correlation between the elements and their function. The specification does not teach what specific components are necessary for detecting mRNA deadenylation and degradation in the assay in which the invention is used. As such, the skilled artisan would not be able to envision what additional components are required detecting mRNA deadenylation and degradation. The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification does not describe what additional components are necessary for detecting mRNA deadenylation and degradation.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. In fact, the specification states that there "is currently no direct biochemical evidence for decapping in mammalian cells" (see paragraph [0007]), therefore it would also lack teachings on detecting mRNA deadenylation and degradation *in addition* to decapping, as claimed. As such, the skilled artisan cannot rely on the prior art to find out what additional components are required for detecting mRNA deadenylation and degradation. Thus, the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the prior art to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches what elements of a mammalian cellular extract are required for decapping. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 8 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims read on a composition or kit comprising any mammalian cell cytoplasmic extract, a methylated cap analog and a cap-labeled mRNA substrate, wherein said extract is depleted of protein activity for polyadenylate binding. The claims read on a broad genus of proteins from any source that may bind polyadenylate.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims depleting any mammalian cell cytoplasmic extract for any protein that binds polyadenylate by function only, without any disclosed information about the proteins that bind polyadenylate in any source of mammalian cell extracts. The specification only provides teachings regarding the use of competitor poly(A) sequences to deplete this activity in S100 HeLa cell extracts. As such, the skilled artisan would not be able to envision how to deplete other mammalian cell extracts of proteins having the activity to bind polyadenylate.

The prior art does not provide sufficient information on the subject to overcome the written description requirements. There does not appear to be any description of depleting any other mammalian cell extracts of proteins with the activity to bind polyadenylate. As such, the skilled artisan cannot rely on the prior art to envision the invention as claimed.

Neither the specification of the instant application or the prior art teaches the depletion of proteins with the activity to bind polyadenylate from a mammalian cellular extract other than an S100 HeLa cell extract. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore

applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 8, 13 and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "mammalian cell lysate" in the first line of the claim. There is insufficient antecedent basis for this limitation in the claim. Changing the claim to read "mammalian cell extract" would be remedial.

The term "depleted of activity" in claim 8 is a relative term which renders the claim indefinite. The term "depleted of activity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear from the claim what level of activity represents "depleted."

The term "pyrimidine rich element" in claim 13 is a relative term which renders the claim indefinite. The term "pyrimidine rich element" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what percentage of pyrimidines in a sequence constitutes a "pyrimidine rich element."

Claims 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. The claim is directed toward a kit for *in vitro* mammalian mRNA decapping. The claim as it reads describes a kit that is necessary for mammalian mRNA decapping to occur. It appears that the claim should be directed towards a kit that *measures* mRNA decapping *in vitro*.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-6, 9, 10, and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohno *et al.* (*Nuc. Acids Res.* **18**(23): 6989-6995, 1990; see entire document).

Ohno *et al.* teaches a cytoplasmic S100 HeLa cell extract containing a capped mRNA and a methylated cap analog for competition experiments (see for example the Abstract). The high-salt washed cytoplasmic extract is centrifuged at 100,000 x *g* (see p. 6990, left-side, second paragraph). The capped RNA is synthesized using [α-^{32}P]-GTP as a label (see for example page 6991, left side, second paragraph). The cap analog used was 7-methyl GTP (see for example page 6991, right side, first full paragraph).

Claims 1, 4-6, 9, 10 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hellmann *et al.* (*J. Biol. Chem.* **257**(8): 4056-4062, 1982; see entire document).

Hellmann *et al.* teaches a cytoplasmic reticulocyte cell extract containing a capped mRNA and a methylated cap analog for competition experiments (see for example the Abstract). In the RNA binding assay, ^{32}P was used to label the cap (see for example page 4057, left side, last paragraph). The cap analog used was 7-methyl GTP (see for example page 4057, left side, first paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ohno *et al.* as applied in the rejections of claims 1, 2, 4-6, 9, 10, and 17-20 under 102(b) above, in view of Robyt *et al.* (Biochemical Techniques: Theory and Practice, ISBN 0-534-07944-X (1987); see for example pages 263, 264 and 271).

Ohno *et al.* teaches a cytoplasmic S100 HeLa cell extract containing a capped mRNA and a methylated cap analog for competition experiments (see for example the Abstract). The high-salt washed cytoplasmic extract is centrifuged at 100,000 x *g* and diluted into 10% glycerol (see p. 6990, left-side, second paragraph). The capped RNA is synthesized using [α-^{32}P]-GTP as a label (see for example page 6991, left side, second paragraph). The cap analog used was 7-methyl GTP (see for example page 6991, right side, first full paragraph).

Ohno *et al.* does not teach the dialysis of the extract.

Robyt *et al.* teaches dialysis, that it can be used to remove small molecules from samples (see for example page 263) and that dialysis is a step in general extract purification schemes to remove excess salt (see for example page 271).

It would have been obvious to the ordinary skilled artisan to combine these teachings in because Ohno *et al.* is purifying an extract having a high salt-wash (centrifugation) and storing it in glycerol, and it was known that dialysis could decrease the salt concentration of the extract. It would have been obvious to dialyze against glycerol because Ohno *et al.* teaches storing their extract in glycerol. The ordinary skilled artisan would have been motivated to combine these teachings to remove salt contamination of the extract prior to its storage. Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
December 16, 2002

PATENT EXAMINER